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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,292	07/05/2005	Susumu Muto	P26318	5595

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EXAMINER
RAE, CHARLESWORTH E

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
10/06/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/516,292	MUTO ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 28-41* is/are pending in the application.

4a) Of the above claim(s) *30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 28-29, 32-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 07/0808, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Status of the Claims

Claims 1, and 28-41 are currently pending in this application.

Claims 30-31 are withdrawn for examination purposes for being directed to non-elected subject matter.

Claims 1, 28-29, and 32-41 are presented for examination.

Amendment

Applicant's claim amendment filed 07/08/08 is acknowledged. Applicant's statement that support for the amendments may be found in the specification as filed is also acknowledged (see applicant's Response, received 07/08/08, at pages 26-44)

Response to applicant's arguments/remarks

Objection

The objection is rendered moot by the claim amendment canceling claim 19l.

Rejection under 112, 2nd para.

This rejection is withdrawn in view of the claim amendment.

Scope of enablement rejection under 112, 1st paragraph

Applicant's argument are not found to be sufficiently persuasive to overcome the rejection for the reasons made of record in the Office action, mailed 01/08/08, at pages 5-11 and for the additional reasons set forth below (see applicant's Response, at pages 45-46):

a) It is noted that each US application/patent is prosecuted on its own merits. Therefore, the prosecution history of the US Patent 6,492,425 (Callahan et al.) enabled the terms "solvates/hydrates" and applicant has not provided any persuasive arguments or evidence to overcome the rejection. further, it is noted that the Callahan et al. is directed to a different scope and compound even though the compounds are similar, however, the difference in the compound claimed is what determines enablement.

Lack of written description under 112, 1st paragraph

Applicant's arguments are not found to be sufficiently persuasive to overcome the rejection for the reasons made of record in the Office action, mailed 01/08/08, at pages 11-13, and for the additional reasons set forth below (see applicant's Response, at pages 46-47):

a) It is noted that each US application/patent is prosecuted on its own merits. Therefore, the prosecution history of the US Patent 6,492,425 (Callahan et al.) enabled the terms "solvates/hydrates" as well as provide wirtten description for said terms. Further, applicant has not provided any persuasive arguments or evidence to overcome

the rejection. In addition, it is noted that the Callahan et al. is directed to a different scope and compound even though the compounds are similar, however, the difference in the compound claimed is what determines enablement and written description.

Nonstatutory obviousness-type double patenting (ODP) rejection

This rejection is withdrawn in view of applicant's persuasive arguments.

Rejection under 103(a)

Applicant contends that this rejection should be withdrawn (see applicant's Response, pages 48-49).

In response, this rejection is withdrawn in view of applicant's persuasive arguments.

NEW REJECTIONS

Claim Rejections – 35 USC 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 28-29, and 32-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for methods of treating/reducing cancer cell

growth or proliferation comprising administering to a subject in need thereof of an effective amount of the compounds of formula 1, does not reasonably provide enablement for methods of completely inhibiting or completely preventing any and all cancer cell growth or any solvates or hydrates of compound of formula I. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth in *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman* 230 USPQ 546 (BdApls 1986) at 547 the court cited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art.

Nature of the invention

The invention in general relates to a method for prophylactic and/or therapeutic treatment of tumor in a mammal including a human, which comprises the step of administering a prophylactically/inhibiting or therapeutically effective amount of a compound of general formula I as recited in claim 1, …hydrate thereof, and solvate thereof".

State and predictability of the art

Slater (Slater S. Non-curative chemotherapy for cancer- is it worth it? Clinical Medicine. 2001;1(No. 2): 220-222) teaches that most patients with cancer achieve only

modest prolongation of survival and limited improvements in the quality of life (page 220, first para.). Slater teaches that drug resistance and the non-selectivity of current conventional therapies limit their use. Slater postulates that with increased funding, and increased awareness of the potential benefits of treatment, could result in real optimism in cancer care (page 222, last para.). Thus, there is reasonable doubt that most tumors/cancers can by prevented or cured.

Vippagunta et al. (Vippagunta et al. Crystalline solids. Advanced Drug Delivery Reviews. 2001;48:3-26) teach that the current focus of research in the solid-state area is to understand the origins of polymorphism at the molecular level and to predict and prepare the most stable polymorph of a drug (abstract). Vippagunta et al. teaches that different crystalline polymorphs and solvates differ in crystal packing, and/or molecular conformation as well as in lattice energy and entropy and that there are usually significant differences in the physical properties (page 4, col. 2, last para.). Besides various pharmaceutical processes during drug development significant influence the final crystalline form of the drug in the dosage form (page 5, col. 1, first full para.). Thus, there is reasonable doubt regarding whether the solvates and hydrates of the compounds encompassed by instant claim 1, for example, would exhibit the same pharmaceutical/pharmacokinetic properties of the non-solvate and non-hydrate form of said compounds.

Relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. It is noted that the chemical and clinical oncological arts are generally unpredictable, requiring each embodiment to be individually assessed for chemical, pharmacologic, pharmaceutical, and clinical efficacy. The more unpredictable an area, the more specific enablement is necessary in order to satisfy the statue. (see *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)).

The breadth of the claims

The instant claims are relatively broad in scope. For example, claim 1 recites the term *"[a] method for prophylactic or therapeutic treatment of tumor in a mammal"* is very broad and encompasses, for example, normal healthy individuals without any evidence of cancer/tumor. Further, the term "tumor" encompasses a multiplicity of different clinically distinct conditions, wherein treatment of one condition (e.g. hormonally sensitive breast cancer) may not be effective in treating another (e.g. non-hormonally sensitive breast cancer). In addition, claim 1, for example, recite the terms "hydrate thereof" and "solvate thereof," which when viewed in light of the specification and the state of knowledge of art raises doubt regarding the predictability in formulating solvates or hydrates of the multiplicity of compounds encompassed by formula I Because the therapeutic response to be achieved would necessarily vary depending upon the specific tumor, which would reasonably vary with the specific chemical compound species of formula I, the level of predictably in practicing the claimed invention would be greatly diminished.

The amount of direction or guidance provided and the presence or absence of working examples

The specification discloses 268 specific compounds of the general formula I (63-99). Applicant discloses that generally the dose of the compound may be 0.01 to 5,0000 mg per day, and when used as an injection may be given 0.001 to 100 mg per day for an adult when used as an injection (page 105, first full para). Also, applicant discloses in vitro and mouse study data (Examples 1-6, pages 193-196), wherein the IC IC50 (μM) for various compounds against certain cancer cell lines is disclosed; namely, Jurkat, MIA Paca-2, HepG2, B16 melanoma, HT-1080 fibrosarcoma, NB-1 neuroblastoma, HMC-1-8 breast cancer cells (see pages 193-196, including Examples 1-6). In particular, Example 6 exemplifies an inhibitory test against cancer cell proliferation of HepG2 (human liver cancer), A549 (human lung cancer), MIA PACA-2 (human pancreatic cancer) wherein the 50% inhibitory concentration IC50 (μM), for example, for Compound 4 (i.e. HepG2 = 0.72; A549 4.03; MIA PaCa-2 0.82), versus, for example, Compound 192 (i.e. HepG2 = 11.02; A549 =23.91; MIA PaCa-2 9.42) are provided (see page 195). Based on the instant disclosure, the applicant at best has provided specific direction or guidance only for a general method of preventing tumors. No reasonably specific guidance is provided concerning useful prophylactic protocols (e.g. dosages) or specific agents for preventing all cancers. Further, extrapolation of the exemplified in vitro data and in vivo data disclosed by applicant to a

human model would reasonably require extensive experimentation to establish a correlation between the structure-activity data and the multiple contemplated treatment effects to be achieved in practicing the instant claimed invention.

The quantity of experimentation necessary

In view of the uncertainty and unpredictability of the art as evidenced by the discussion of the prior art, it is reasonable to surmise that this level of uncertainty in the art would require one skilled in the art to conduct more than routine experimentation in order to practice the claimed invention commensurate with the scope of the claims.

For the reasons stated above, claims 1, 28-29, and 32-41 are rejected under 35 USC 112, first paragraph, for lack of scope enablement because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Claims 1, 28-29, and 32-41 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 1, 28-29, and 32-41 are directed to encompass compounds solvates and hydrates of said compounds

which only correspond in some undefined way to specifically instantly disclosed chemicals. None of the undisclosed solvate or hydrate compounds meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the disclosed chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

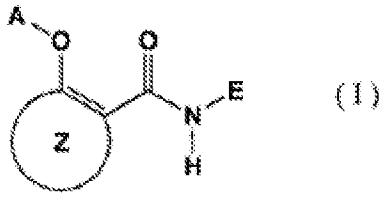
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 28-29, and 32-41 are rejected under 103(a) as being unpatentable over Franz et al. (US Patent 3,906,034), in view of Callahan et al. (US Patent 6,492,425).

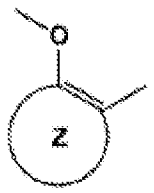
Claim 1 recites "[a] method for prophylactic or therapeutic treatment of tumor in a mammal including a human, which comprises the step of administering a prophylactically or therapeutically effective amount of a substance selected from the group consisting of a compound represented by the following general formula (I), a pharmacologically acceptable salt thereof, and a hydrate thereof, a hydrate thereof, and a solvate thereof:



(I)

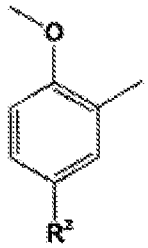
wherein A represents a hydrogen atom or an acetyl group, E represents a 2,5-di or a 3,5-di-substituted phenyl group, wherein at least one of said substituents is a trifluoromethyl group, and the other substituent is selected from the group consisting of a halogen atom, a nitro group, an alkyl group, …, a carboxy group, and a monycyclic

non-aromatic heterocyclic group which may substituted with one or more halogenated alkyl groups, or …" Claim 28 recites "wherein the tumor is selected from the group consisting of skin cancer, melanoma, kidney cancer, lung cancer, ..." Claim 29 recites "wherein the mammal is a human." Claim 32 recites "[a] method for prophylactic or therapeutic treatment of cancer in a mammal including a human, which comprises the step of administering a prophylactically or therapeutically effective amount …" Claim 34 recites "[a] method for inhibiting proliferation of tumor cell or cancer cell, …" Claim 35 recites "wherein E is a 2,5- or 3,5-disubstituted phenyl group ..." Claim 36 recites "wherein E a is 3,5-bis(triflurоromethyl)phenyl group, a 3-fluoro-5)trifluoromethyl)phenyl group, a 3-bromo-5-(trifluoromethyl)phenyl group, a 3-methoxy-5-(trifluoromethyl)phenyl group, ..." Claim 37 recites "wherein Z is a benzene ring which may have one or more substitutents independently selected from the group consisting of a halogen atom, a nitro group, a cyano group, an alkoxy group, ..." Claim 38 recites "wherein the following partial formula (Iz-1) in the general formula containing ring Z



(Iz-1)

is represented by the following formula (Iz-2):

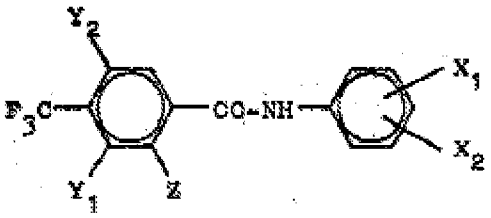


(Iz-2)

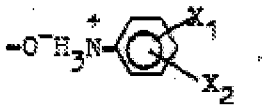
wherein Rz represents a hydrogen atom, a halogen atom, a nitro group, …" Claim 39 recites "wherein Rz is a hydrogen atom, a halogen atom, a nitro group, a cyano group, and alkoxy group, …" Claim 40 recites "wherein Rz is a hydrogen tom, a halogen atom, a nitro, a cyano group, a methody group, a methyl group, …" Claim 41 recites "wherein A is hydrogen atom, E is a 2,5- or 3,5-di-substituted phenyl group wherein at least one of said substitutents is a trifluoromethyl group, and the other substituent is selected from the group consisting of a halogen atom, a halogenated alkyl group, an alkoxy group, or a di-substituted thiazol2-yl group wherein said substitutents are independently selected from the group consisting of an alkyl group, a halogenated alkyl group, a cyano group, an aryl group, …, ring Z is a benzene ring which may have one or more substituents …"

Franz et al. (US Patent 3,906,034) teach compounds having the below general structure and methods comprising administering said compounds either orally or

subcutaneously for treating warm blooded animals suffering from helminthiasis (abstract; col. 3, line 24 to col. 4, line 26:

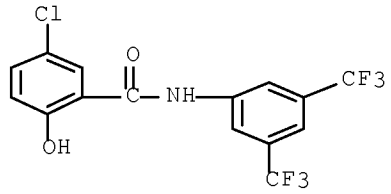


in which X_1 and X_2 each represent hydrogen, chlorine, methyl or trifluoromethyl, Y_1 and Y_2 each represent hydrogen, chlorine or the nitrogroup, at least one of the substituents Y_1 and Y_2 not being hydrogen, and Z stands for —OH, —O—CO—alkyl or



The above structure taught by Franz et al. overlaps with the compounds encompassed by instant claimed formula I, as recited for example in claim 1, when reference X1 and X2 are trifluoromethyl (= bis-trifluoromethyl phenyl; equivalent to the E moiety recited in instant formula I), reference Y1= hydrogen, reference Y2 = chlorine, and reference Z = OH). However, unlikenlike the instant claimed compounds, Franz et al. teach compounds that have an additional trifluoromethyl substituent on the phenyl ring equivalent to the instant claimed Z ring, which is represented below:

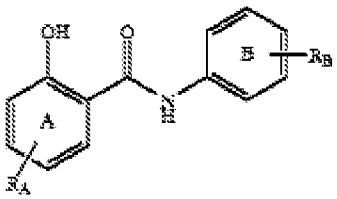
RN 978-62-1 CAPLUS, CN Benzamide, N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2 hydroxy- (CA INDEX NAME), wherein the corresponding structure is shown below:



Also, Franz et al. do not teach a method for prophylactic or therapeutic treatment of tumors.

Callahan et al. (6,492,425) is added for its teaching of methods of treating cancer comprising compounds wherein a major portion of said compounds is identical to the instant claimed compounds. Callahan et al. teach the below inhibitory compounds of transcription factor NF-κB and methods of treatment of a variety of diseases associated with NF-κB activation in a patient in need of treating, including cancer (e.g. Hodgkin's disease) and restenosis, wherein the patient includes human (see abstract, and col. 3, line 17 to col. 4, line 54; see especially reference claim 1):

I



wherein:

R_A substitutes ring A 0–3 times and is independently selected from the group consisting of: NO_2, halogen, C_{1-6}alkyl, trifluoromethyl, O—C_{1-6}alkyl and S—C_{1-6}alkyl; and

R_B substitutes ring B 0–3 times and is independently selected from the group consisting of: halogen,C(O)

C_{1-6}alkyl, C_{1-6}alkyl, O—C_{1-6}alkyl, S—C_{1-6}alkyl, CH_2-aryl, and aryl;

Unlike the instant claimed compounds, Callahan et al. do not teach compounds wherein the ring B substituents (= equivalent to instant claimed E) comprise trifluoromethyl groups.

It would have been obvious to a person of skill in the art at the time the invention was made to treat a mammal, including a human, with cancer (= tumor) as taught by Callahan et al. by administering a pharmaceutically active preparation comprising a compound taught by Franz et al., including applicant's elected compound species, to reduce the growth/proliferation of cancer/cancer cells. One would have been motivated to treat a human with cancer with a pharmaceutically active preparation comprising a compound taught by Franz et al., including applicant's elected compound species, to reduce the growth/proliferation of the cancer/cancer cells because Callahan et al. teach compounds wherein a major portion of said compounds is identical to the compounds taught by Franz et al. and applicant's elected compound which are useful for treating

cancer. One would have expected to successfully treat a human with cancer with a compound as taught by Franz et al., including applicant's elected compound species, because Callahan et al. and Franz et al. teach compounds wherein a major portion of said compounds is identical and therefore a person of skill in the art would expect compounds that possess similar structures to exhibit similar spectrum of pharmacological/therapeutic activity. Besides, it is routine in the chemical arts to modify the substituents of phenyl rings to determine the structure-function relationships between different functional groups. Hence, the combination of the cited prior art teach methods of treatment comprising administering pharmaceutically active compounds which are capable of performing the desired function.

Thus, a person of skill in the art at the time the invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

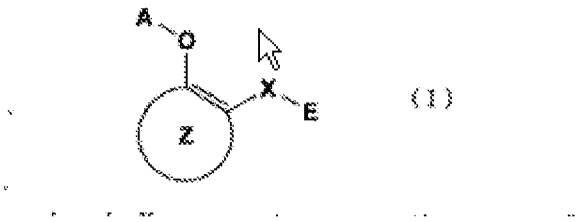
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 18-24, and 28-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17, 21, 24-33 of copending U.S. Patent Application No. 10/564, 407 (appl. '407), in view of Callahan et al. (US Patent 6,492,425). The above discussion of Callahan et al. is incorporated by reference.

In particular, claim 1 of copending appl. '407 is directed towards a medicament for preventive and/or therapeutic treatment of dermal pigmentation and/or development

of skin cancer, which comprises as an active ingredient a substance selected from the group consisting of a compound represented by the below general formula (I):



(I)

wherein X represents a connecting group whose number of atoms in a main chain is 2 to 5 (said connecting group may be substituted), A represents hydrogen atom or acetyl group, E represents an aryl group which may be substituted or a heteroaryl group which may be substituted, ring Z represents an arene which may have one or more substituents in addition to the group represented by formula -- O-A wherein A has the same meaning as that defined above and the group represented by formula --X--E wherein each of X and E has the same meaning as that defined above, or a heteroarene which may have one or more substituents in addition to the group represented by formula --O--A wherein A has the same meaning as that defined above and the group represented by formula -- X--E wherein each of X and E has the same meaning as that defined above. Unlike the instant claims, the reference claims are limited in scope to a method for preventive and/or therapeutic treatment of dermal conditions.

It would have been obvious to a person of skill in the art at the time the invention was made to treat a patient with cancer as taught by Callahan et al. with the reference

method comprising administering the identical compounds as recited in the instant claims for its anti-tumor effect. One would have been motivated to treat any cancer with said reference method because Callahan et al. teach similar compounds that are useful for treating cancer. Thus, a person of skill in the art at the time the invention was made would have considered the instant claimed invention to be an obvious variant of the reference claims.

Claims 1, 28-29, and 32-41 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 13-14, 19-23, 25-30, 55-63 of copending US Patent Application No. 10/433,619, in view of Callahan et al. (US Patent 6,492,425). Unlike the instant claims, the reference claims are directed to a method of inhibiting activation of NF-kB comprising administering the identical instantly claimed compounds of formula 1. The above discussion of Callahan et al. is incorporated by reference. To reiterate, Callahan et al. teach inhibitory compounds of transcription factor NF-κB and methods of treatment of a variety of diseases associated with NF-κB activation in a patient in need of treatment thereof, including cancer (e.g. Hodgkin's disease) and restenosis, wherein the patient includes human (see abstract, and col. 3, line 17 to col. 4, line 54; see especially reference claim 1. It would have been obvious to a person of skill in the art at the time the invention was made to treat a patient with an NF-κB associated disorder (e.g. Hodgkin's disease) as taught by Callahan et al. with a reference compound to its anti-cancer effect. One would have been motivated to treat a patient in need of treatment thereof with a reference compound because Callahan et al. teach NF-κB inhibitor drugs, wherein a major

portion of the chemical structure of said drugs is identical to the reference compounds, which are useful for treating NF-κB associated disorders and drugs that have similar structures would reasonably be expected to exhibit similar therapeutic profiles. Thus, the instant reference claims are found to be an obvious variant of the reference claims.

These are provisional obviousness-type double patenting rejections because the conflicting claims of the copending applications have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the

Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12 September 2008

/C. R./

Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611